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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,187	07/30/2001	Rosanne M. Crooke	ISPH-0590	2706

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MARY E. BAK
HOWSON AND HOWSON, SPRING HOUSE CORPORATE CENTER
BOX 457
SPRING HOUSE, PA 19477

EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,187	CROOKE ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,9,10 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,9,10 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 13, 2004 has been entered.

Claims 1, 4-7, 9, 10 and 12-15 are pending in the application.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 4-7, 9, 10 and 12-15 under 35 USC 112, first paragraph, made in the previous office action is withdrawn in view of the amendments made to the claims on 9/13/2004.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 4-7, 9, 10 and 12-15 under 35 USC 102 (b) as being anticipated by Damha et al. or Biegelman et al. are withdrawn in view of the amendments made to the claims on 9/13/2004.

Claim Rejections - 35 USC § 103

Claims 1, 4-7, 9, 10 and 12-15 are rejected under 35 USC 103(a) as unpatentable over Stenn et al. in view of and Baracchini et al. and McKay et al. (US 6,030,837, February 29, 2000).

Claims 1, 4-7, 9, 10 and 12-15 are drawn to an antisense compound 20 nucleotides in length targeted to a nucleic acid encoding human stearoyl-coA desaturase, wherein the antisense comprises modified bases, including 5-methylcytosine modifications, modified sugars, including 2'-O-methoxyethyl modifications, internucleoside linkage modifications, including phosphorothioate, chimeric antisense, and compositions comprising said antisense and a pharmaceutically acceptable carrier, including a colloidal dispersion system. The claims are further drawn to methods for inhibiting the expression of human stearoyl-coA desaturase in cells *in vitro*.

Stenn et al. teaches inhibition of expression of human stearoyl-coA desaturase using antisense expressed from a vector and teaches the full length sequence of a nucleic acid encoding human stearoyl-coA desaturase, wherein the nucleic acid comprises SEQ ID NO: 3 of the instant application (see, for example, figures 8 and 9 of Stenn et al.). Specifically, Stenn et al. teach at page 31:

> "This invention still further provides an expression vector suitable for use in gene therapy, which vector encodes a nucleic acid molecule capable of specifically inhibiting the expression of human skin stearoyl-coA desaturase. In one embodiment, the nucleic acid molecule is an anti-sense molecule which is complementary to, and specifically hybridizes with, at least a portion of human stearoyl-coA desaturase MRNA."

Stenn et al. do not teach antisense targeted to a nucleic acid encoding human stearoyl-coA desaturase that are 20 bases in length. Stenn et al. do not teach antisense targeted to a nucleic acid encoding human stearoyl-coA desaturase wherein the antisense comprises a modified backbone, a modified sugar, a 5-methylcytosine modified base or chimeric antisense molecules.

Baracchini et al. and McKay et al. both teach backbone modifications for antisense, including phosphorothioate modifications, 2'-O-methoxyethyl sugar modifications, 5-methyl cytosine base modifications, chimeric oligonucleotides and modified internucleoside linkages, including phosphorothioate linkages, to increase antisense stability and enhance affinity of antisense oligonucleotides 8-30 nucleotides in length. Baracchini et al. and McKay et al. further teach pharmaceutical carriers and colloidal dispersion systems (for example liposomes) for use in delivery of antisense compounds.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of full-length antisense to human stearoyl-coA desaturase and the sequence of the cDNA of this gene taught by Stenn et al. with the antisense oligonucleotides having the length and modifications taught by Baracchini et al. and McKay et al.

A person of ordinary skill in the art would have been motivated to combine the teachings of Stenn et al. with the teachings of Baracchini et al. and McKay et al. because Stenn et al. teach inhibiting human stearoyl-coA desaturase using antisense and one of ordinary skill in the art would be motivated to make such antisense with a

length of 20 nucleobases for ease of synthesis and delivery and because it is conventional in the art to make antisense within this range (as exemplified by both Baracchini et al. and McKay et al.). One of ordinary skill in the art would have been motivated to incorporate the modifications taught by Baracchini et al. and McKay et al. for the benefits of stability and improved hybridization. Baracchini et al. and McKay et al. each provide general teachings of antisense design which parallel the general teaching of the instant specification and teach antisense oligonucleotides that are 20 bases in length and inhibit their respective targets by more than 10%. For example, see Table 1 of McKay et al. and column 11, lines 2-8 of Baracchini et al.

It would have been obvious to one of ordinary skill in the art to use antisense targeted to a nucleic acid encoding human stearoyl-coA desaturase in a method of inhibiting the expression of human stearoyl-coA desaturase in cells *in vitro*, because it would be an obvious use for an antisense molecule designed to hybridize to and inhibit the expression of a nucleic acid encoding human stearoyl-coA desaturase.

Therefore, the invention of claims 1, 4-7, 9, 10 and 12-15 would have been obvious to one of ordinary skill in the art, as a whole, at the time the instant invention was made.

Response to Arguments

Applicant's arguments in the remarks submitted September 13, 2004 have been fully considered but are not persuasive. The examiner agrees with the applicant's statement that combination of these references would not provide the present

application. However, combination of these references does teach the claimed invention. Applicant asserts that the combination of Stenn et al., Milner et al. and Baracchini et al. does not provide one of ordinary skill in the art with a reasonable expectation of success in providing antisense sequences that would inhibit expression of human stearoyl CoA desaturase and that the examiner is applying an improper "obvious to try" standard. Applicant further asserts that Stenn et al. do not teach antisense to human stearoyl CoA desaturase, cannot suggest 20mer antisense oligonucleotides and provides no basis for an expectation of inhibition of the desaturase enzyme by any percentage. This is not persuasive because, in fact, Stenn et al. clearly teach antisense to human stearoyl CoA desaturase as described in the previous 103 rejection and provide an expectation of inhibition on page 27:

> "In the instant cell-based methods, the amount by which the H-SCD expression level is increased or decreased can be any quantifiable amount. In the preferred embodiment, this amount is at least a 50% increase or decrease in expression level"

The assertion that Stenn et al. does not suggest 20mer antisense sequences is not persuasive because although the teaching of Stenn et al. does not specifically teach 20mers, neither does it recite any size limit for the antisense oligonucleotides and therefore encompasses antisense sequences of any length.

Applicant asserts that neither Baracchini et al. nor Milner et al. provide a teaching of antisense inhibition of human stearoyl CoA desaturase. This is not a persuasive argument because the art is taken as a whole, not individually, to teach inhibition of human stearoyl CoA desaturase using oligonucleotides containg base, sugar and internucleoside linkages. Baracchini et al. teach modifications to antisense

oligonucleotides that are conventional in the art and are used via well-known synthetic methods to produce antisense oligonucleotides with superior physical properties.

Far from not providing a reasonable expectation of success in combining the teachings of Stenn et al. and Baracchini et al., Baracchini et al. actually provide the person of ordinary skill in the art with a further expectation of success; teaching numerous antisense oligonucleotides 20 bases in length, indicating this is a length routinely used in the field of antisense. Baracchini et al. also provide general teachings of antisense design which parallel the instant specification and show antisense oligonucleotides that are 20 bases in length and inhibit their targets by more than 10%. If applicant believes that 10% inhibition of human stearoyl CoA desaturase is an unexpected result, they are invited to provide evidence to support this belief.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
November 5, 2004

SEAN McGARRY
PRIMARY EXAMINER
1635